

Somatosensory impairments in the upper limb post stroke: distribution and association with motor function and visuo-spatial neglect

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Abstract

Background: A thorough understanding of the presence of different upper limb somatosensory deficits post stroke and the relation with motor performance remains unclear. Additionally, knowledge about the relation between somatosensory deficits and visuo-spatial neglect is limited.

Objective: To investigate the distribution of upper limb somatosensory impairments and the association with uni- and bimanual motor outcome and visuo-spatial neglect.

Methods: A cross-sectional observational study was conducted including 122 patients within 6 months after stroke (median 82 days, IQR 57-133 days). Somatosensory measurement included the Erasmus modified Nottingham sensory assessment (Em-NSA); perceptual threshold of touch (PTT); thumb finding test; two-point discrimination, and stereognosis subscale of the NSA. Upper limb motor assessment comprised the Fugl-Meyer assessment, motricity index, action research arm test and adult-assisting hand assessment stroke. Screening for visuo-spatial neglect was performed using the star cancellation test.

Results: Upper limb somatosensory impairments were common, with prevalence rates ranging from 21-54%. Low to moderate Spearman rho correlations were found between somatosensory and motor deficits ($r=.22$ - $r=.61$), with the strongest associations for PTT ($r=.56$ - $r=.61$) and stereognosis ($r=.51$ - $r=.60$). Visuo-spatial neglect was present in 27 patients (22%). Between-group analysis revealed significantly more often and more severe somatosensory deficits in patients with visuo-spatial neglect ($p<0.05$). Results showed consistently stronger correlations between motor and somatosensory deficits in patients with visuo-spatial neglect ($r=.44$ - $r=.78$) compared to patients without neglect ($r=.08$ - $r=.59$).

Conclusions: Somatosensory impairments are common in sub-acute patients post stroke and related to motor outcome. Visuo-spatial neglect was associated with more severe upper limb somatosensory impairments.

Key words: Stroke, Upper Extremity, Somatosensory Impairment, Motor Deficit, Visuo-spatial Neglect

Introduction

The somatosensory system allows us to interpret somatosensory stimuli received from receptors located in the joints, ligaments, muscles and skin.¹ Somatosensory information such as pain, pressure or joint position sense, is then processed in different brain regions to modulate incoming sensory information.¹ Key brain regions involved in processing somatosensory information are the primary and secondary somatosensory cortex, the thalamus, insula, posterior parietal cortex and the cerebellum.² Within the somatosensory system, a classification in exteroceptive, proprioceptive and higher cortical somatosensation can be identified.^{3,4} Each of these categories include a set of somatosensory modalities such as light touch and pain within exteroceptive somatosensation, position and movement sense within proprioceptive somatosensation and somatosensory discrimination sense within higher cortical somatosensation.³ Deficits of these somatosensory modalities are common after stroke, with prevalence rates ranging from 11% to 85%.⁵⁻⁷ Variability is attributed to differences in definition, study populations, somatosensory modalities tested, and assessment method used.⁵ To date, most studies concentrated on identifying deficits in a single somatosensory modality such as light touch perception or joint position sense. Therefore, a thorough understanding of the prevalence and distribution of deficits in different exteroceptive, proprioceptive and higher cortical somatosensory modalities in the sub-acute phase post stroke is lacking.

Along with upper limb somatosensory impairments, approximately 70% of patients post stroke experience motor impairments in the affected upper limb.⁸ Our recent systematic review⁹ investigating the impact of somatosensory deficits on outcome after stroke, showed that different somatosensory impairments are negatively associated with motor recovery in

the upper limb. Despite these results, the review highlighted the need for large high-quality cohort studies that combine somatosensory measures of different modalities to determine the relationship with both unimanual and bimanual motor performance with more accuracy.

It is well known from previous literature that visuo-spatial neglect, a neuropsychological disorder often encountered post stroke, negatively affects recovery.¹⁰⁻¹⁶ Unilateral visuo-spatial neglect has been defined as the inability to detect, respond to, and orient towards novel and significant stimuli occurring in the hemi space contralateral to a brain lesion.¹⁷ The reported incidence of neglect ranges between 10% and 80% of the stroke survivors.^{18,19} Variability among studies is again believed to be related to subject selection, nature and timing of the assessment and differences in definitions of this complex phenomenon.²⁰ It was recently shown that the time course of recovery of visuo-spatial neglect mimics the recovery patterns of other neurological impairments such as motor or functional outcome, with large improvements in the first weeks post stroke, and with the recovery reaching a plateau around three months post stroke.²¹ Visuo-spatial neglect is known to increase length of hospital stay¹¹, may hinder response to therapy¹¹ and is negatively associated with performance in activities of daily living.¹² Nijboer et al.¹³ showed that on admission to the rehabilitation centre, patients with visuo-spatial neglect have significantly worse functional performance compared to patients without neglect, as measured with the Barthel Index and Functional Independence Measure (FIM).¹³ A detailed analysis of the different domains of the functional independence measure showed that on average, patients with neglect scored significantly lower on self-care, transfers and locomotion compared to the non-neglect patients, whereas no differences were found between groups for sphincter control and cognition.¹³

Furthermore, visuo-spatial neglect is linked to poor motor performance^{13,15,16} and has a suppressive effect on upper limb motor recovery, mainly during the first three months post stroke, when spontaneous neurological recovery is taking place.¹⁴ Despite the shared neuro-anatomy between somatosensory processing and the presence of visuo-spatial neglect in areas of the parietal cortex,^{22,23} only a few studies^{13,14,24-27} reported the relationship between visuo-spatial neglect and somatosensation in the upper limb. The presence of visuo-spatial neglect seems to be associated with more severely affected limb position sense in the arm,^{13,14,25-27} and is predictive for impaired limb movement sense.²⁴ However, information on the association between visuo-spatial neglect and exteroceptive or higher cortical somatosensory deficits after stroke is lacking.

The primary objectives of this study were therefore (1) to map the prevalence and distribution of different exteroceptive, proprioceptive and higher cortical somatosensory impairments in the upper limb and (2) to study the association between different somatosensory impairments and unimanual as well as bimanual motor function post stroke. A final objective was to investigate whether the presence of neglect is associated with the occurrence (3a) and severity (3b) of somatosensory impairments, and whether the association between somatosensory impairments and unimanual as well as bimanual motor outcome is different for patients with and without visuo-spatial neglect (3c). The primary hypothesis was that, in line with previous literature,⁵⁻⁷ upper limb somatosensory deficits are common, and that from the group of somatosensory impairments, higher cortical somatosensory deficits are most prevalent. This hypothesis is driven by the fact that for higher cortical sensation such as discrimination of different objects, an intact exteroceptive sensation (i.e. touch and pressure) as well as higher cortical discriminative function is required.⁶ Secondly, based on a recent systematic review completed by the investigators,⁹ it was hypothesized that somatosensory

impairments are moderately associated with uni- and bimanual motor function. Thirdly, based on the closely related neuro-anatomy,^{2,22,23} it was further hypothesized that visuo-spatial neglect is highly associated with the prevalence and severity of exteroceptive, proprioceptive and higher cortical somatosensory deficits. Finally, based on the previously completed systematic review⁹ we expect that somatosensory deficits are moderately associated with uni- and bimanual motor function, equally in patients with and without visuo-spatial neglect.

Methods

Participants

Inclusion and exclusion criteria. For this cross-sectional observational study, one hundred twenty-two (n=122) patients were assessed between October 2013 and August 2014 in seven neurorehabilitation units in Belgium (n=102) or in the home environment of the patient (n=20). Patients assessed in the home environment all completed inpatient rehabilitation, and were still enrolled in outpatient physical therapy. The inclusion criteria were: (1) first-ever stroke as defined by the World Health Organization (WHO)²⁸; (2) assessed within the first six months after stroke; (3) motor and/or somatosensory impairment in the upper limb, using outcome measures as described below; (4) minimally 18 years old, and; (5) substantial cooperation to perform the assessment. Patients were excluded if they had: (1) a pre-stroke Barthel index²⁹ score of < 95 out of 100; (2) other neurological impairments with permanent damage such as multiple sclerosis or Parkinson's disease; (3) a subdural hematoma, tumor, encephalitis or trauma that led to similar symptoms as a stroke, and; (4) serious communication, cognitive or language deficits, which could hamper the assessment. Subjects signed a written informed consent form prior to participation. Ethical approval was obtained from the Ethics Committee of the University Hospital of Leuven, and all participating centers.

Patients were assessed in a single test session. One trained researcher performed the data collection. Patients' baseline characteristics were assessed, including age at stroke onset, gender, comorbidities (cumulative illness rating scale, CIRS³⁰), hand dominance, time post stroke, lateralization and type of stroke.

Outcome measures

Somatosensory assessment

Exteroceptive somatosensation

The *Erasmus MC modification of the (revised) Nottingham sensory assessment* (Em-NSA)³¹ assesses light touch, pressure and pinprick. Light touch was applied with a cotton wool, pressure with the index finger and pinprick with a toothpick, at predefined points. Scores for each modality range from 0 (loss of somatosensory function) to 8 (intact somatosensory function). A cut-off score of <7 indicates the presence of somatosensory impairment. The Em-NSA has good to excellent intra-rater and inter-rater reliability.³¹

The *perceptual threshold of touch* (PTT)³² is the minimal stimulus level of touch that is detectable. A transcutaneous electric nerve stimulation (TENS) was applied with a portable device: A CEFAR Primo Pro (Cefar Medical AB, Sweden). Round electrodes, with a diameter of 3 cm, were applied to the index finger and bulb of the thumb. A high-frequency constant current of 40Hz with single square pulses of 80 μ s pulse duration is applied. The amplitude is gradually increased with increments of 0.5mA, until a tingling sensation is being perceived at the index finger. Good psychometric properties are established for the PTT.³² To evaluate the PTT impairment, individual scores were compared to age- and gender-matched cut-off norm-values.³³

Proprioceptive somatosensation

The *Erasmus MC modification of the (revised) Nottingham sensory assessment* (Em-NSA)³¹ assesses proprioception by passively moving predefined joints of the upper limb. Scores range from 0 (loss of proprioceptive function) to 8 (intact proprioceptive function). A cut-off score of <7 indicates the presence of proprioceptive impairment (movement sense). The Em-NSA has good to excellent intra-rater and inter-rater reliability.³¹

The *thumb finding test* (TFT)³⁴ was used to evaluate proprioception, as it examines the ability to locate the thumb of the affected limb in space. The scoring ranges from 0 (no difficulty) to 3 (severe difficulty). A cut-off score of >0 indicates the presence of impaired proprioception (position sense).

Higher cortical somatosensation

The *Erasmus MC modification of the (revised) Nottingham sensory assessment* (Em-NSA)³¹ assesses sharp-dull discrimination by alternating sharp (toothpick) and dull (finger) stimuli, at predefined points. Scores range from 0 (loss of discriminative function) to 8 (intact discriminative function). A cut-off score of <7 indicates the presence of higher cortical somatosensory impairment. The Em-NSA has good to excellent intra-rater and inter-rater reliability.³¹

During the *stereognosis assessment* of the original NSA,³⁵ patients need to identify 11 everyday objects by touch and manipulation in the affected hand, while blindfolded. Assistance to manipulate the objects in the hand is given by the assessor, when needed. For each object a score from 0 (failed to recognize object) to 2 (recognized object) is given. A cut-off score of <19 indicates the presence of stereognosis impairment. The stereognosis section of the NSA shows a moderate to good test-retest reliability in patients with stroke.³⁶

Two-point discrimination (2PD)³⁷ was assessed at the fingertip of the index finger. Distance between the points was gradually reduced from 15 mm until the patient incorrectly felt only one point. The last correct answer was recorded as the result. The 2PD threshold in healthy controls has a mean of 3.5 mm (\pm SD 1.7).³⁸ Subjects with a two-point discrimination threshold higher than 5 mm were classified as having impaired 2PD. Good reliability has been found for the 2PD assessment.³⁷

In summary, based on the different assessments, exteroceptive somatosensation included the measures of light touch, pressure and pinprick (of the Em-NSA), and the perceptual threshold of touch. Proprioceptive somatosensation was assessed using the thumb finding test and the proprioception subscale of the Em-NSA. Finally, higher cortical somatosensation comprised of sharp-dull discrimination, stereognosis and two-point discrimination.

Assessment of visuo-spatial neglect

The Star Cancellation Test (SCT)³⁹ from the Behavioural Inattention Test (BIT)⁴⁰ was used to assess the presence of visuo-spatial neglect. A previous study⁴¹ found the SCT to be the most sensitive paper-and-pencil measure of visuo-spatial neglect. Different stimuli are presented on a piece of paper, including large stars, letters, short words and small stars. The test page is placed at the patient's midline. The task is to locate and cross out all small stars using their hand of choice. A cut-off score of <44 (out of 54 stars) indicates the presence of visuo-spatial neglect.⁴² A lateralization index was calculated from the ratio of stars cancelled on the left of the page to the total number of stars cancelled, according to Halligan et al.⁴³ Laterality scores range from 0 to 1 with values near 0.5 suggesting unbiased performance, between 0 and 0.46 indicating visuo-spatial neglect in the left hemispace and between 0.54 and 1 indicating visuo-spatial neglect in the right hemispace. Interrater reliability of the SCT is found to be high.⁴⁴

Motor assessment

The Fugl-Meyer assessment upper extremity (FMA-UE)⁴⁵ is a reliable and valid measure for overall motor impairment, with a total score between zero and 66. The *action research arm test* (ARAT)⁴⁶ measures motor performance in 4 different subscales: grasp, grip, pinch and gross movement, with a maximum score of 57. Reliability⁴⁷ and validity⁴⁸ are

established for the ARAT. *The arm section of the motricity index* (MI)⁴⁹ is a reliable measure of muscle strength during pinch grip, flexion of the elbow and abduction of the shoulder. Total scores vary between 0 and 100. The *adult assisting hand assessment stroke* (Ad-AHA Stroke), a Rasch-based performance scale, measures how effectively the affected hand is spontaneously used during performance of a bimanual task. Performance of the semi-structured present-task was video-recorded. Nineteen test items, describing different object-related hand actions are scored on a 4-point scale rating the quality of performance. The raw scores are then converted through the Rasch analysis to logit-scores varying between 1 and 100, with higher scores indicating higher bimanual ability levels (unpublished results).⁵⁰

Statistical analysis

Patients' clinical and demographic characteristics were displayed as frequencies with percentage, mean with standard deviation (SD) and median with interquartile range (IQR). The prevalence and distribution of deficits in different somatosensory modalities such as light touch, position sense or stereognosis, were calculated using frequencies with percentages according to the presence of exteroceptive, proprioceptive or higher cortical somatosensory problems. Therefore, the different somatosensory variables were dichotomized according to the presence of a deficit or normal functioning based on the above mentioned predefined cut-off values. Furthermore, associations between somatosensory and motor impairments were assessed using Spearman rank correlation coefficients. For this analysis, the full score range of the somatosensory and motor variables were used. Strength of the relation was interpreted according to Munro's correlation descriptors⁵¹: very low: $r = 0.01-0.24$, low: $r = 0.25-0.49$, moderate: $r = 0.50-0.69$, high: $r = 0.70-0.89$ and very high: $r = 0.90-1.00$.

To study the relation with neglect, first, all clinical and baseline characteristics from patients with visuo-spatial neglect were compared to patients without visuo-spatial neglect by using Wilcoxon rank sum test and Chi square tests. Second, the prevalence of somatosensory deficits in patients with visuo-spatial neglect was compared to the prevalence in patients without visuo-spatial neglect by using Chi Square tests. Severity of different somatosensory impairments was compared between patients with and without visuo-spatial neglect, using the Wilcoxon rank sum test. Finally, using the Fisher r-to-z transformation, it was tested whether the correlation coefficients for the association between somatosensory and motor impairments found in the patients with and without neglect were significantly different. P-values were considered statistically significant at the 0.05 level. All statistical analyses were performed using SPSS, version 22.

Results

One hundred twenty-two patients (n=122) were assessed from 12 days until six months post stroke (median 82 days, IQR 57-133). Table 1 shows the patient characteristics, presented for the total group, for the patients with visuo-spatial neglect (n=27, 22%) and without visuo-spatial neglect (n=95, 78%). For the total group, median age at stroke onset was 67 years (IQR 59-76) and 63% of the patients were males. The majority of patients suffered from ischemic stroke (88.5%). A total of 48 patients (39%) showed right-sided hemiparesis, 73 patients (60%) left-sided, and one patient had symptoms at both sides of the body.

[Insert Table 1]

Total group

Objective 1: Map prevalence and distribution of different somatosensory impairments

In the total group, exteroceptive impairments (light touch, pressure, pinprick, light touch threshold) were present in 21-37% of the patients, with the perceptual threshold of touch (PTT) revealing the highest frequency (37%) of exteroceptive dysfunction. Proprioceptive impairment (position sense, movement sense) was diagnosed in 23% of the patients when using the Em-NSA, whereas 54% of the patients showed proprioceptive impairment using the thumb finding test. Finally, deficits in higher cortical somatosensation (sharp-dull discrimination, stereognosis, two-point discrimination) were present in 43-50% of the patients (Figure 1, panel A). Panel B shows the distribution of somatosensory impairments according to the presence of unique (pure) exteroceptive, unique proprioceptive or unique higher cortical somatosensory impairments or a mixture of these deficits. This shows that only 16% of the patients presented without somatosensory impairment, and that approximately

50% of the patients experienced a mixture of somatosensory impairments. Therefore, only a minority of patients had unique exteroceptive (14%), unique proprioceptive (9%) and unique higher cortical somatosensory (13%) impairments.

[Insert Figure 1]

Objective 2: Study sensorimotor associations

Table 2 shows results of the correlation analysis between somatosensory and unimanual (FMA-UE, MI, ARAT) and bimanual (Ad-AHA Stroke) motor assessment for the total group. Overall, low correlations ($r=.22$ - $r=.44$) were found between somatosensory and motor deficits, except for the perceptual threshold of touch (PTT) and stereognosis which showed moderate correlations with motor function ($r=.51$ - $r=.61$). For each of the somatosensory variables, comparable results were found for the association with unimanual and bimanual motor function.

[Insert Table 2]

Between-group differences in patients with and without visuo-spatial neglect

Objective 3a: Map prevalence and distribution of somatosensory deficits

Twenty-seven patients had visuo-spatial neglect, with a median score on the SCT of 29 (IQR 18-33). Twenty patients had visuo-spatial neglect in the left hemispace, four in the right hemispace and three had non-lateralised visuo-spatial neglect. As seen in table 1, patients with visuo-spatial neglect had significantly more often right hemisphere lesions and significantly more severe unimanual (FMA-UE, MI, ARAT) and bimanual (Ad-AHA Stroke) motor scores compared to patients without neglect. Figure 2 shows the prevalence (panel A)

and distribution (panel B) of somatosensory impairments for patients with and without visuo-spatial neglect. Patients with neglect have significantly ($p<0.05$) more often somatosensory impairments (prevalence 41% to 78%) compared to patients without neglect (prevalence 15% to 47%) (Figure 2, panel A). The distribution analysis presented in panel B showed that in the neglect group, 7.4% had no somatosensory impairment, which is considerably less compared to the no-neglect group (18.9%). Furthermore, 74.1% of the patients with visuo-spatial neglect presented with mixed exteroceptive, proprioceptive or higher cortical somatosensory impairments, whereas only 40% presented with mixed impairments in the no-neglect group.

[Insert figure 2]

Objective 3b: Assess severity of somatosensory impairments

Significant between-group differences in severity of the different somatosensory impairments are shown in Table 3. Exteroceptive (light touch, pressure, pinprick, light touch threshold), proprioceptive (position sense, movement sense) and higher cortical somatosensory (sharp-dull discrimination, stereognosis, two-point discrimination) functions were significantly ($p<0.05$) more severely affected in patients with visuo-spatial neglect.

[Insert Table 3]

Objective 3c: Study sensorimotor associations

The correlation analysis between somatosensory and uni- and bimanual assessment in patients with and without visuo-spatial neglect revealed overall stronger correlations in the neglect group ($r=.44$ - $r=.78$) compared to the no-neglect group ($r=.08$ - $r=.59$) (Table 4), with statistically significant between-group differences for the correlation of all motor scores

(except for the ARAT), with stereognosis and pressure. On the other hand, the correlation between the perceptual threshold of touch (PTT) and all four motor outcomes, was comparable for patients with neglect ($r=.46$ - $r=.55$) and without neglect ($r=.55$ - $r=.59$). Furthermore, the association between somatosensory deficits and unimanual outcome (ARAT, FM-UE, MI) was comparable to the association with bimanual outcome (Ad-AHA Stroke). Finally, the highest values in correlation coefficients were found for the association between stereognosis and motor function in patients with neglect ($r=.72$ - $r=.78$) as well as without neglect ($r=.40$ - $r=.51$).

[Insert Table 4]

Discussion

Results of this study showed that deficits in upper limb somatosensation are common in patients in the sub-acute phase post stroke and that these deficits are associated with unimanual and bimanual motor performance. It was shown that patients with neglect have more combined and more severe exteroceptive, proprioceptive and higher cortical somatosensory deficits compared to patients without neglect. Furthermore, this study showed that in patients with neglect, consistently stronger associations exist between somatosensory impairments and unimanual and bimanual motor performance, compared to patients without neglect.

Results of the study regarding the prevalence of somatosensory deficits are in line with previous studies. Connell et al.⁶ reported that 23-47% experienced exteroceptive impairments in the upper limb, 43-63% proprioceptive impairments, and stereognosis was affected in 31-89% of the patients on admission to the rehabilitation centre. Tyson et al.,⁷ reported that from a group of patients two to four weeks post stroke, 55% had exteroceptive dysfunction, whereas only 22% had proprioceptive dysfunction in the upper limb. This result might be explained by the inclusion of solely patients with an anterior circulation stroke, resulting primarily in deficits in the lower limb. Furthermore, the proprioceptive integration areas, located in the posterior parietal lobe in the brain,⁵² were probably not affected by lesions in the anterior circulation. Interestingly, this study showed a large difference in prevalence of proprioceptive deficits when using the thumb finding test (54%) compared to the proprioception subscale of the Em-NSA (23%). This latter result might be explained by the difference in assessment methods. During the thumb finding test (TFT), position sense of the whole upper limb is assessed which might be more difficult compared to selective assessment of movement sense in separate joints in the Em-NSA.

As expected from our recent systematic review⁹, this study showed that different somatosensory deficits are associated with motor impairments in the upper limb, especially the perceptual threshold of touch (PTT) and stereognosis, which showed moderate correlations with motor function. For each of the somatosensory variables, comparable results were found for the association with unimanual and bimanual motor function.

As hypothesized, the study showed that patients with visuo-spatial neglect present with more mixed somatosensory impairments and significantly more severe somatosensory impairments, compared to the no-neglect group. This finding could be explained by the extent of the lesion, as larger lesions will affect motor, somatosensory and attention areas in the brain. Patients with neglect had indeed, besides worse somatosensory outcomes, consistently worse motor outcomes. This might provide indirect evidence of larger brain lesions in patients with visuo-spatial neglect. Brain regions important in somatosensory processing, are also in close proximity to brain regions responsible for neglect. In a study of Ptak et al.,²³ visuo-spatial neglect was associated with damage to the temporal-parietal junction, the middle frontal gyrus and the posterior intraparietal sulcus, whereas Yue et al.,⁵³ showed that lesions in the inferior frontal gyrus, pre- and postcentral gyrus, superior and middle temporal gyrus, the insula and surrounding white matter, were more frequent in patients with visuo-spatial neglect compared to patients without neglect. These regions are in close proximity to the brain areas responsible for the processing of different somatosensory inputs such as the primary and secondary somatosensory cortex, insula and posterior parietal cortex.²

We acknowledge that the presence of visuo-spatial neglect might interfere with the assessment of somatosensory functioning due to the attention deficit. Therefore, the fact that patients with neglect have more mixed and more severe somatosensory impairments might also be attributed to the attention deficit. However, neglect was assessed using the SCT, a test for visuo-spatial extra-personal neglect, which is distinct from personal neglect,^{22,54-56} of

which the latter plausibly more strongly interferes with somatosensory testing. Furthermore, the sample group included patients with visuo-spatial neglect without any somatosensory deficit, which supports that somatosensory function in patients with visuo-spatial neglect can be tested. Future research could use an integrative approach, combining different measures of neglect to capture all different dimensions of personal and extra-personal neglect using different paper-and-pencil tests and an extensive behavioral assessment such as the Catherine Bergego scale to study neglect during activities of daily living.⁵⁵⁻⁵⁷

Interestingly, the study also showed that in patients with neglect, the association between somatosensory and uni- and bimanual motor outcome is moderate to strong, compared to only low to moderate in the no-neglect group with significant between group differences for stereognosis and pressure perception. These findings may be important when delineating rehabilitation strategies, as patients with neglect might benefit from other types of treatment. Somatosensory function showed to be equally associated with both unimanual and bimanual motor performance. Finally, stereognosis showed to have the strongest association with motor function. This last finding is in accordance with results of a study of Connell et al.,⁶ in which upper limb performance was found to be a significant predictor of stereognosis impairment. This correlation is not surprising as the recognition of objects relies on manual exploration to derive meaningful knowledge about the characteristics of the object. Assistance to manipulate the objects in the hand is given by the assessor, however it remains unclear whether patients derive the necessary perceptions by this method. Future studies are needed to gain insights in the validity of the stereognosis assessment in patients with severe hand paresis.

The strength of the current study is that it included the use of a combination of reliable and valid assessment methods for different somatosensory modalities of exteroceptive, proprioceptive and higher cortical functioning in a large cohort of subacute stroke patients.

Furthermore, besides the pure clinical assessment methods, an increased objective measure to assess the exteroceptive function was included, namely the perceptual threshold of touch (PTT).³² PTT measures the threshold of light touch in a more sensitive way by using high-frequency TENS which activates cutaneous receptors of light touch and their accompanying large myelinated A β fibres.³² The clinical score of light touch and the PTT scores were significantly correlated ($r=-.63$) but our results suggest that the PTT assessment was able to identify more light touch deficits. This might have contributed to the finding that correlations between PTT and motor performance was the same for patients with and without visuo-spatial neglect. This highlights the potential of PTT as a measure of exteroceptive function in patients post stroke, both for research purposes and the clinical setting.

Some limitations of the study need to be recognized. First, patients were assessed in different settings: 84% of our patients were assessed in seven different rehabilitation centers and 16% were assessed at home but were still enrolled in outpatient physical therapy. Recruitment of patients was not consecutively, but was conducted in the different rehabilitation centers, upon eligibility on predefined assessment days. A flowchart cannot be provided as there is no data available on patients who were ineligible for participation in the study. The specific content and frequency of the treatment was not documented and therefore we were not able to control for treatment provided. Secondly, detailed information on localization and extent of the lesion would have been useful in exploring the shared neuro-anatomy between brain areas responsible for the outcomes of the study. Third, measurement of visuo-spatial neglect with solely the Star Cancellation Test (SCT) might be seen as limited in order to assess this complex phenomenon. Yet, the emphasis of this study was on the somatosensory and motor functioning, with visuo-spatial neglect as an influencing factor. Future research is necessary to replicate these findings with a more extended test battery for personal and extra-personal neglect using a combination of different paper-and-pencil tests as

well as behavioural assessment such as the Catherine Bergego Scale to assess neglect in daily activities.⁵⁷ Furthermore, we were not able to control for hemianopia as a confounding factor during the assessment of neglect, which could have influenced the results of the Star Cancellation Test, due to a possible interfering visual impairment. Finally, sub-acute patients were assessed between 12 days and six months after stroke, which covers a broad time window for inclusion of the patients. Of our sample of 122 patients, 57% was in the early sub-acute phase (up to three months post stroke) and 43% was in the late sub-acute phase (between three and six months post stroke). As these groups were not comparable based on the different demographic and clinical characteristics, between-group analyses were not indicated. Future studies should report on repeated assessments at fixed time points.

Conclusions

The novel findings from this large cross-sectional study are that somatosensory deficits are frequently seen in the sub-acute phase post stroke, and related to motor outcome. The presence of visuo-spatial neglect is associated with the presence and severity of somatosensory deficits. Secondly, in patients with neglect, somatosensory impairments have a stronger association with motor impairments, when compared to patients without neglect. Therefore, recommendation for practice includes the screening of visuo-spatial neglect from the early stage post stroke. This might imply that patients with neglect need different intervention strategies for sensorimotor rehabilitation. Furthermore, as this study showed that somatosensory deficits are common after stroke, we suggest the clinical use of reliable and valid measures of somatosensory deficits. Additionally, quantitative measures such as PTT can be helpful in clinical practice.

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Conflict of interest

None

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Figure 1. A) Prevalence of exteroceptive, proprioceptive and higher cortical somatosensory deficits in the upper limb after stroke in all patients; B) distribution of somatosensory deficits: unique (pure) and mixed somatosensory impairments in all patients

Figure 2. A) Prevalence of exteroceptive, proprioceptive and higher cortical somatosensory deficits in the upper limb after stroke in patients with and without visuo-spatial neglect; B) distribution of somatosensory deficits: unique (pure) or mixed somatosensory impairments in patients with and without visuo-spatial neglect

Table 1. Patient Characteristics

	All patients (n=122)	Patients with neglect (n=27)	Patients without neglect (n=95)	p
Age stroke onset: median (IQR)	67 (58.8 -76.1)	68 (60.2-77.7)	66.7 (58.7-75.7)	0.646*
Gender, n (%)				0.376 ⁺
Male	77 (63.1)	19 (70.4)	58 (61.1)	
Female	45 (36.9)	8 (26.6)	37 (38.9)	
Days after stroke, median (IQR)	82 (57-132.8)	94 (64-169)	79 (56-123)	0.209*
Inpatient rehabilitation, n (%)	102 (83.6)	24 (88.9)	78 (82.1)	0.401 ⁺
Lateralisation, n (%)				0.033 ⁺
Right hemiparesis	48 (39.4)	5 (18.5)	43 (45.3)	
Left hemiparesis	73 (59.8)	22 (81.5)	51 (53.6)	
Both	1 (1.8)	0 (0)	1 (1.1)	
Type of stroke, n (%)				0.946 ⁺
Ischemia	108 (88.5)	24 (88.9)	84 (88.4)	
Haemorrhage	14 (11.5)	3 (11.1)	11 (11.57)	
Hand dominance, n (%)				0.251 ⁺
left	8 (6.6)	0 (0)	8 (8.4)	
right	113 (92.6)	27 (100)	86 (90.5)	
both	1 (0.8)	0 (0)	1 (1.1)	
CIRS: median (IQR)	6 (4-8)	7 (4-9)	6 (4-8)	0.244*
SCT: median (IQR)	27 (22.1)	29 (18-33)	52 (50-54)	< 0.001*
FMA-UE: median (IQR)	38 (7-59)	8 (5-58)	43 (10-60)	0.011*
MI: median (IQR)	67.5 (18-8.3)	23 (0-83)	76 (37-84)	0.016*
ARAT: median (IQR)	24.5 (3-54.3)	3 (0-43)	32 (3-56)	0.004*
Ad-AHA Stroke: median (IQR)	50.9 (14-79.8)	11 (0-77.8)	63.9 (17.9-88.4)	0.004*

IQR: interquartile range, CIRS: cumulative illness rating scale, SCT: star cancellation test, FMA-UE: Fugl-Meyer motor assessment upper extremity, MI: Motricity Index, ARAT: Action Research Arm Test, Ad-AHA Stroke: adult-Assisting Hand Assessment Stoke * Wilcoxon rank sum test, ⁺ Chi square test

Table 2. Spearman rho correlation coefficients for association between somatosensory and motor impairments in all patients (n=122)

	FMA-UE	MI	ARAT	Ad-AHA Stroke
Exteroceptive somatosensation				
Em-NSA - Light touch	.309*	.318*	.386*	.372*
Em-NSA - Pressure	.329*	.337*	.382*	.371*
Em-NSA - Pinprick	.337*	.348*	.377*	.367*
PTT - Light touch	-.580**	-.564**	-.611**	-.608**
Proprioceptive somatosensation				
Em-NSA - Movement sense	.412*	.394*	.444*	.422*
TFT - Position sense	-.369*	-.354*	-.365*	-.389*
Higher cortical somatosensation				
Em-NSA - Sharp/dull discrimination	.223	.220	.312*	.282*
NSA - stereognosis	.514**	.535**	.599**	.530**
Two-point discrimination	-.316*	-.316*	-.403*	-.360*

Spearman rho correlation coefficients: Strength of the relation was indicated according to Munro⁴⁹: very low: no indication, low: *, moderate: **, high: ***

FMA-UE: Fugl-Meyer motor assessment upper extremity, MI: Motricity Index, ARAT: Action Research Arm Test, Ad-AHA Stroke: adult-Assisting Hand Assessment Stoke, Em-NSA: Erasmus MC modification of the (revised) Nottingham sensory assessment, PTT: Perceptual threshold of touch, TFT: thumb finding test, NSA: Nottingham sensory assessment

Table 3. Differences in severity of somatosensory impairments in patients with and without visuo-spatial neglect

	Patients with neglect (n=27)	Patients without neglect (n=95)	P
	median (IQR)	median (IQR)	
Exteroceptive somatosensation			
Em-NSA - Light touch	6 (0-8)	8 (7-8)	.000
Em-NSA - Pressure	8 (0-8)	8 (8-8)	.001
Em-NSA - Pinprick	8 (1-8)	8 (8-8)	.002
PTT – Light touch	7 (5-11)	4 (3.5-5.8)	.001
Proprioceptive somatosensation			
Em-NSA - Movement sense	7 (2-8)	8 (7-8)	.000
TFT - Position sense	1 (1-2)	0 (0-1)	.002
Higher cortical somatosensation			
Em-NSA - Sharp/dull discrimination	5 (0-8)	8 (5-8)	.002
NSA - stereognosis	1 (0-19.3)	19 (9.5-21)	.001
Two-point discrimination	16 (5-16)	5 (4-16)	.038

Em-NSA: Erasmus MC modification of the (revised) Nottingham sensory assessment, PTT: perceptual threshold of touch, TFT: thumb finding test, NSA: Nottingham sensory assessment, IQR: interquartile range

Table 4. Spearman rho correlation coefficients for association between somatosensory and motor impairments in patients with and without visuo-spatial neglect

	FMA-UE			MI			ARAT			Ad-AHA Stroke		
	Neglect	No neglect	Fisher r-to-z p-value	Neglect	No neglect	Fisher r-to-z p-value	Neglect	No neglect	Fisher r-to-z p-value	Neglect	No neglect	Fisher r-to-z p-value
Exteroceptive somatosensation												
Em-NSA - Light touch	.517**	.203	0.110	.546**	.222	0.091	.511**	.307*	0.280	.556**	.257*	0.112
Em-NSA - Pressure	.574**	.137	0.024	.588**	.132	0.018	.572**	.214	0.059	.609**	.183	0.023
Em-NSA - Pinprick	.511**	.169	0.085	.565**	.164	0.039	.514**	.236	0.153	.598**	.201	0.034
PTT - Light touch	-.522**	-.546**	0.881	-.549**	-.546**	0.984	-.458*	-.593**	0.412	-.547**	-.550**	0.984
Proprioceptive somatosensation												
Em-NSA - Movement sense	.553**	.340*	0.242	.609**	.310*	0.091	.488*	.387*	0.582	.528**	.343*	0.317
TFT - Position sense	-.492**	-.261*	0.238	-.581**	-.234	0.063	-.437*	-.266*	0.395	-.514**	-.297*	0.254
Higher cortical somatosensation												
Em-NSA - Sharp/dull discrimination	.482*	.082	0.054	.495*	.082	0.044	.491*	.196	0.139	.462*	.150	0.129
NSA - stereognosis	.758***	.400**	0.013	.778***	.423*	0.010	.724***	.512**	0.126	.693**	.418*	0.075
Two-point discrimination	-.474*	-.246	0.250	-.477*	-.258*	0.267	-.457*	-.363*	0.624	-.536**	-.281*	0.177

Spearman rho correlation coefficients: Strength of the relation was indicated according to Munro⁴⁹: very low: no indication, low: *, moderate: **, high: ***

FMA-UE: Fugl-Meyer motor assessment upper extremity, MI: Motricity Index, ARAT: Action Research Arm Test, Ad-AHA Stroke: adult-Assisting Hand Assessment Stoke,

Em-NSA: Erasmus MC modification of the (revised) Nottingham sensory assessment, PTT: Perceptual threshold of touch, TFT: thumb finding test, NSA: Nottingham sensory assessment